Response Dated: March 7, 2008

## Amendments To The Specification:

Please amend the Specification to read as follows:

Enter the Sequence Listing accompanying this submission into the Specification of the above-identified application.

Replace Table 1 in the Specification of the above-identified application with the following table:

Table 1. Naturally Occurring Opioid Peptide Sequences.

Peptide	Sequence	Subtype
Met-Enkephalin	YGGFM (SEQ ID NO:2)	μ/δ
Leu-Enkephalin	YGGFL (SEQ ID NO:3)	δ/μ
Dynorphin A	YGGFLRRIRPKLKWNNQ (SEQ ID NO:4)	κ(μ)
Dynorphin B	YGGFLRRQFKVVT (SEQ ID NO:5)	κ(μ,δ)
α-Neoendorphin	YGGFLRKY (SEQ ID NO:6)	κ(μ,δ)
β-Neoendorphin	YGGFLRKYP (SEQ ID NO:7)	κ(μ,δ)
β <sub>h</sub> -Endorphin	YGGFMTSEKSQTPLVTLFKNAIIKNAYKKGE (SEQ ID NO:8)	μ/δ
Peptide E	YGGFMRRVGRPEWWMDYQKRYGGFL (SEQ ID NO:9)	μ/κ
Peptide F	GGEVLGKRYGGFM (SEQ ID NO:10)	_
Nociceptin	FGGFLRRIRPKLKWNNQ (SEQ ID NO:11)	ORL
Deltorphin	YmFHLMD-CONH <sub>2</sub> (SEQ ID-NO:12)	δ
Dermorphins	YaFGYPS-CONH <sub>2</sub> (SEQ ID NO:13)	μ
Morphiceptin	YPFP-CONH2 (SEQ ID NO:[[14]]12)	μ
β-Casomorphin	YPFPGPI (SEQ ID NO:[[15]]13)	μ
Endomorphin-1	YPWF-CONH <sub>2</sub> (SEQ ID NO:[[16]]14)	μ
Endomorphin-2	YPFF-CONH2 (SEQ ID NO:[[17]]15)	μ
Rubiscolin-6	YPLDLF (SEQ ID NO:[[18]]16)	δ

Application No. 10/540,443
Reply to Office Communication Dated: January 25, 2008

Response Dated: March 7, 2008

Replace paragraph [00018] in the Specification of the above-identified application with the following paragraph:

[00018] The classic motif for opioid receptor binding is the YGGF (SEQ ID NO:1) sequence. While some variations are possible in this motif, it appears that the first tyrosine and the fourth phenylalanine are invariant requirements of enkephalins. The discovery of natural opioid peptides in the skin of the frog *Phyllomedusa bicolor*, which naturally produces the enantiomeric D-amino acids, led to investigations of other D-amino acids which can substitute for the glycine intermediate residues in the motif. In particular, the several motifs with a D-amino acids, including Tyr-D-Cys-Gly-Phe-(SEQ-ID-NO:19), Tyr-D-Ala-Gly-Phe-(SEQ-ID-NO:20), and Tyr-D-Thr-Gly-Phe-(SEQ-ID-NO:21) have been found effective synthetic enkephalin message sequences. Synthetic enkephalin analogues with a D-amino acid substituted for the first glycine have been designed to bias the conformation of the molecule to obtain greater affinity for opioid receptors. Note that in the Table 1 above and 2 below that the small case letter designation refers to a D-amino acid, such as "t" referring to D-Thr.

Replace Table 2 in the Specification of the above-identified application with the following table:

## TABLE 2

			Recept	Receptor Binding Characteristics	g Chara	cteristic	s.				
ID Code	Message		Address		Delta	MU	Delta MU MVD	GPI	ICV(Mouse)	IV(Mouse)	+ Err (95%)
		(Trans)	Transport Sequence)		Ma	Mn Mn	Ma	Mn	IC50 nmol	umol/kg	µmol/kg
Morphine	Morphine	forphine Morphine	hine						2.7	6.3	4.9-7.9
SAM 995	YIGFL	S-CONE	'IGFL S-CONH2 (SEQ ID NO:22)		2.1	7.5	2.723	25.04	0.07	46.4	35.4-60.7
SAM 1095	YtGFL I	L-Ser (b-	L-Ser (b-Glc) CONH2-(SEQ-II) NO:23)		2.37	7.63	1.56	33.83	0.02	11.4	8.5-15.2
MMP 2120	YtGFL I	L-Ser (a-	L-Ser (a-Man) CONH2-(SEQ-ID-NO:24)		22.95	15.2	3.029	23.25	0.04	31.6	26.5-37.8
MMP 2200		L-Ser (b.	L-Ser (b-Lactose) CONH2 (SEQ ID NO:2:	æ	17.3	9	5.727	34.75	0.02	3.2	2.5-4.2
MMP 2205	_	L-Ser, L	L-Ser, L-Ser (b-Glc) CONH2-(SEQ ID-NG	9:50			1.169	53.51	0.3	140.8	78-253.9
MMP 2230		L-Ser (b.	L-Ser (b-Maltose) CONH2 (SEQ ID NO:27)	Œ	986	30.8	1.705	52.57	0.07	~12	
MMP 2300	YtGFL 1	L-Ser (b.	L-Ser (b-Maltotriose) CONH2 (SEQ ID N	O:28)	3.8	15	7.73	71.73	90.0	10.9	8.5-13.9
CM 100		L-Ser (b.	L-Ser (b-Xyl) CONH2 (SEQ ID NO:29)						~0.04	9.45	8.34-10.71
MD 2005		L-Ser (b.	L-Ser (b-Melibiose) CONH2 (SEQ ID NO:30	<b>1</b>	9.6	36.6			0.034	2.16	1.84-2.53
MD 100H	YtGFL I	PNLBE	NLBEKALKS*L-CONH2 <del>(SEQ ID NO:31</del>	<del>1</del> 6					~0.03		
MD 105H	YtGFL (	(beta-Ali	beta-Ala)NLBEKALKS*L-CONH2-(SEQ-II	COM COLOR	9 47.3	62.1			~0.03		
MD 110H	YtGFL (	GGNLB	3GNLBEKALKS*L-CONH2 <del>-(SEQ ID NO:33)</del>	0:33)	35	81			~0.03		